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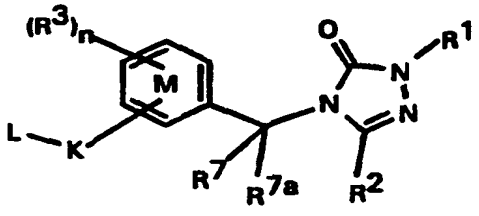
(54) Title: PESTICIDAL 4–BENZYL–1,2,4–TRIAZOLIN–5–ONE DERIVATIVES

(57) Abstract

The invention provides compounds of general formula (I) having pesticidal, especially fungicidal, insecticidal and acaricidal, act ivity.



(I)

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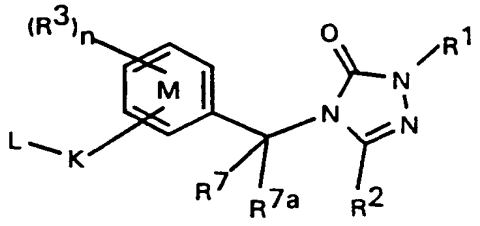
PESTICIDAL 4-BENZYL-1,2,4-TRIAZOLIN-5-ONE DERIVATIVES

This invention relates to compounds having pesticidal, esp cially fungicidal, insecticidal and acaricidal, activity.

According to a first aspect, the invention provides compounds of general formula I



(I)

wherein;

R^1 is optionally substituted alkyl;

R^2 is optionally substituted alkyl, halogen, $-OR^4$, $-SR^4$, $-S(O)R^4$, $-S(O)_2R^4$ or $-NR^5R^6$;

n is 0 to 4;

each R^3, which may be the same or different from each other, is optionally substituted alkyl or halogen;

R^7 and R^{7a}, which may be the same or different are, optionally substituted alkyl, acyl, halogen or cyano;

K is -O-, $-S(O)_p$-, -C(=O)-, $-NR^8$-,

$-CHR^9-A^1(C=A^2)-A^3-$, $-CHR^9-O-N=C(R^{10})-A^4-$, $-C(=O)NR^8-$,

$-O-CH_2CH_2O-N=C(R^{10})-$, $-CHR^9O-C(R^{10})=N-$, $-CHR^9S-C(R^{10})=N-$,

$-C(R^{10})=N-N(R^8)-$, $-CH=N-N=C(R^{10})-$, $-CHR^9N(R^8)-N=C(R^{10})-$,

$-CHR^9N[C(=O)R^{11}]-N=C(R^{10})-$, $-OC(=S)NR^8C(=O)-$, $-CHR^9-C(=A^2)-A^3-$,

$-CHR^9CHR^{12}-C(=A^2)-A^3-$, $-CR^{10}=CR^{13}-C(=A^2)-A^3-$, $-C\equiv C-C(=A^2)-A^3-$,

$-N=CR^{10}-C(=A^2)-A^3-$, $-CH(OR^{11})-$, $-CHR^9-$, $-CHR^9CHR^{12}-$, $-CR^{10}=CR^{13}-$,

$-C\equiv C-$, $-CHR^9O-$, $-OCHR^9-$, $-CHR^9S(O)_p-$, $-S(O)_pCHR^9-$,

$-(R^{10})C=N-OCH(R^9)-$, $-C(R^{10})=N-O-$, $-O-N=C(R^{10})-$, $-CHR^9SC(R^{10})=N-NR^8-$,

$-CHR^9SC(R^{10})=N-N=CR^{13}-$, $-CHR^9OC(R^{10})=N-N=CR^{13}-$ or a direct bond;

where the moiety depicted on the right side of the linkage is attached to L; and

L is optionally substituted alkyl; optionally substituted alkenyl; optionally substituted alkynyl; optionally substituted heterocyclyl; optionally substituted carbocyclyl, preferably optionally substituted phenyl; or $Si(R^{15})_3$; or one R^3, K and L, together with the phenyl ring M, form an optionally substituted fused ring, which may contain heteroatoms;

where R^4 is hydrogen or optionally substituted alkyl;

R^5 and R^6, which may be the same or different, are hydrogen or optionally substituted alkyl, or R^5 and R^6 taken together with the nitrogen to which they are attached may form a heterocyclyl group, preferably a 5 to 7-membered heterocyclyl group, which may be substituted and may contain other hetero atoms, for example morpholino, thiomorpholino or piperidinyl;

p is 0 to 2;

A^1 is -O-, -S-, $-NR^8-$ or $-O-N(R^8)-$;

A^2 is O, S or NR^8;

A^3 is -O-, -S-, $-NR^8-$ or a direct bond;

A^4 is $-NR^8-$, $-OCH_2-$, -(C=O)-, $-CH_2O-$, $-CH_2S-$ or a direct bond;

R^8 is hydrogen, optionally substituted alkyl, optionally substituted carbocyclyl or optionally substituted heterocyclyl;

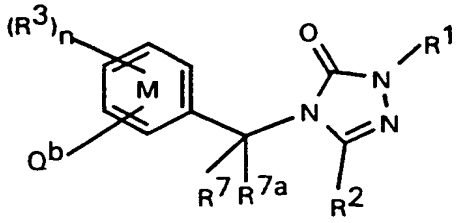
R^9 and R^{12}, which may be the same or different, are hydrogen, optionally substituted alkyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, $-NR^5R^6$, cyano, halogen or nitro;

R^{10} and R^{13}, which may be same or different, are hydrogen, optionally substituted alkyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted alkenyl, optionally substituted alkynyl, acyl, $-OR^4$, $-S(O)_pR^4$, $-NR^5R^6$, nitro, halogen or cyano, wherein when K is $-CHR^9SC(R^{10})=N-N=CR^{13}-$, R^{10} is preferably $-SR^4$;

R^{11} is hydrogen, optionally substituted alkyl or optionally substituted carbocyclyl; and

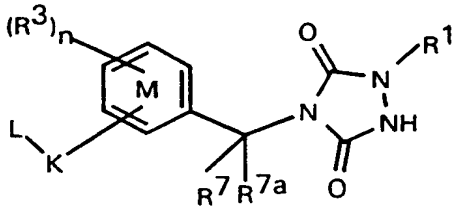
R^{15} is alkyl.

Some novel compounds of general formula I have weak pesticidal activity but still have utility as intermediates and such compounds also form part of the invention. Therefore, according to another aspect the invention provides as reaction intermediates, compounds of formula II, wherein Q^b is a leaving group, preferably a halogen such as bromine, and R^1, R^2, R^3, R^7 and R^{7a} are as defined above.



(II)

According to another aspect the invention provides as reaction intermediates, compounds of formula III, wherein R^1, R^3, R^7, R^{7a}, L and K are as defined above.



(III)

Any alkyl group present in the molecule may be straight or branched and is preferably of 1 to 10 carbon atoms, especially 1 to 7 and particularly 1 to 5 carbon atoms.

Any alkenyl or alkynyl group may be straight or branched and is preferably of 2 to 7 carbon atoms and up to 3 double or triple bonds which may be conjugated, for example vinyl, allyl, butadienyl or propargyl.

Any reference to the term carbocyclyl or carbocyclic includes saturated carbocyclyl groups; unsaturated carbocyclyl groups having up to 3 double bonds, which may be conjugated; and aromatic carbocyclyl groups, e.g. phenyl. Carbocyclyl groups are typically 3 to 8 membered rings. In addition, the term carbocyclyl includes fused carbocyclyl groups, e.g. napthalene, phenanthrene, indane and indene.

Any reference to the term heterocyclyl or heterocyclic includes both aromatic and non-aromatic heterocyclyl groups. Heterocyclyl groups are generally 5, 6 or 7-membered rings containing up to 4 hetero atoms selected from nitrogen, oxygen and sulfur.

Examples of heterocyclyl groups are furyl, thienyl, pyrrolyl, pyrrolinyl, pyrrolidinyl, imidazolyl, dioxolanyl, oxazolyl, thiazolyl, imidazolyl, imidazolinyl, imidazolidinyl, pyrazolyl, pyrazolinyl, pyrazolidinyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, thiadiazolyl, pyranyl, pyridyl, piperidinyl, dioxanyl, morpholino, dithianyl, thiomorpholino, pyridazinyl, pyrimidinyl, pyrazinyl, piperazinyl, sulfolanyl, tetrazolyl, triazinyl, azepinyl, oxazepinyl, thiazepinyl, diazepinyl and thiazolinyl. In addition, the term heterocyclyl includes fused heterocyclyl groups, for example benzimidazolyl, benzoxazolyl, imidazopyridinyl, benzoxazinyl, benzothiazinyl, oxazolopyridinyl, benzofuranyl, quinolinyl, quinazolinyl, quinoxalinyl, dihydroquinazolinyl, benzothiazolyl, phthalimido, benzofuranyl, benzodiazepinyl, indolyl and isoindolyl.

Any alkyl, alkenyl, alkynyl, carbocyclyl, heterocyclyl group, when substituted, may be substituted by at least one group, which may be the same or different, and may be selected from the group: nitro; halogen; cyano; acyl; -O-acyl; -S-acyl; optionally substituted carbocyclyl; optionally substituted heterocyclyl; $-SF_5$; $-Si(R^a)_3$, where R^a is optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl and optionally substituted heterocyclyl; $-OR^b$ and $-SR^b$ where R^b is the same as R^a or hydrogen; NR^cR^d where R^c and R^d, which may be the same or different, are hydrogen, optionally substituted alkyl, acyl, or R^c and R^d taken together with the nitrogen to which they are attached form a heterocyclyl group, preferably a 5 to 7-membered heterocyclyl group, which may be substituted and may contain other hetero atoms, for example morpholino, thiomorpholino or piperidinyl. Any carbocyclyl or heterocyclyl groups may also be substituted by optionally substituted alkyl, optionally substituted alkenyl and optionally substituted alkynyl. Particularly preferred substituents on any alkyl, alkenyl or alkynyl group are halogen, alkoxy, haloalkoxy, alkylthio or optionally substituted phenyl. Particularly preferred substituents on any carbocyclyl or heterocyclyl group are as defined above for alkyl, alkenyl or alkynyl, and also alkyl and haloalkyl.

The term acyl includes the residue of sulfur and phosphorus-containing acids as well as carboxylic acids. Examples of acyl groups are: $-C(=O)R^e$, $-C(=O)OR^e$, $-C(=E)NR^eR^f$, $-C(=O)N(R^e)OR^f$, $-C(=O)ONR^eR^f$, $-C(=O)N(R^e)NR^fR^g$, $-C(=O)SR^e$,

$-C(=S)SR^e$, $-S(O)_pR^e$, $-S(O)_2OR^e$, $-S(O)_pNR^eR^f$, $-P(=E)(OR^e)(OR^f)$, and $-C(=O)-C(=O)OR^e$; where p is 1 or 2; E is O, S or, where appropriate, NR^e or NOR^e; and where R^e, R^f and R^g, which may be the same or different, are as defined for R^b hereinabove, or R^e and R^f, or R^f and R^g, together with the atom(s) to which they are attached may form a ring, preferably a 5 to 7-membered heterocyclyl group which may be substituted and may contain other hetero atoms.

In cases where the compounds of the invention exist as the E and Z isomers, the invention includes individual isomers as well as mixtures thereof.

The compounds of the invention have activity as fungicides, especially against fungal diseases of plants, e.g. mildews and particularly barley powdery mildew (*Erysiphe graminis*) and vine downy mildew (*Plasmopara viticola*), rice blast (*Pyricularia oryzae*), cereal eyespot (*Pseudocercosporella herpotrichoides*), rice sheath blight (*Pellicularia sasakii*), grey mould (*Botrytis cinerea*), damping off (*Rhizoctonia solani*), wheat brown rust (*Puccinia recondita*), late tomato or potato blight (*Phytophthora infestans*), apple scab (*Venturia inaequalis*), glume blotch (*Leptosphaeria nodorum*). Other fungi against which the compounds may be active include other powdery mildews, other rusts, and general pathogens of Deuteromycete, Ascomycete, Phycomycete and Basidomycete origin.

The compounds of the invention also have insecticidal, acaricidal and nematicidal activity and are particularly useful in combating a variety of economically important insects, acarids and plant nematodes, including animal ectoparasites and especially Diptera, such as sheep blow-fly, *Lucilia sericata*, and house-flies, *Musca domestica*; Lepidoptera, including *Plutella xylostella*, *Spodoptera littoralis*, *Heliothis armigera* and *Pieris brassicae*; Homoptera, including aphids such as *Megoura viciae*; Coleoptera, including corn rootworms (*Diabrotica* spp., e.g. *Diabrotica undecimpunctata*); and spider mites, such as *Tetranychus* spp..

The invention thus also provides a method of combating pests (i.e. fungi, insects, nematodes, acarids and weeds) at a locus infested or liable to be infested therewith, which comprises applying to the locus a compound of formula I.

The invention also provides an agricultural composition comprising a compound of formula I in admixture with an agriculturally acceptable diluent or carrier.

The composition of the invention may of course include more than one compound of the invention.

In addition the composition can comprise one or more additional active ingredients, for example compounds known to possess plant-growth regulant, herbicidal, fungicidal, insecticidal or acaricidal properties. Alternatively the compound of the invention can be used in sequence with the other active ingredient.

The diluent or carrier in the composition of the invention can be a solid or a liquid optionally in association with a surface-active agent, for example a dispersing agent, emulsifying agent or wetting agent. Suitable surface-active agents include anionic compounds such as a carboxylate, for example a metal carboxylate of a long chain fatty acid; an *N*-acylsarcosinate; mono- or di-esters of phosphoric acid with fatty alcohol ethoxylates or salts of such esters; fatty alcohol sulfates such as sodium dodecyl sulfate, sodium octadecyl sulfate or sodium cetyl sulfate; ethoxylated fatty alcohol sulfates; ethoxylated alkylphenol sulfates; lignin sulfonates; petroleum sulfonates; alkyl-aryl sulfonates such as alkyl-benzene sulfonates or lower alkylnaphthalene sulfonates, e.g. butyl-naphthalene sulfonate; salts of sulfonated naphthalene-formaldehyde condensates; salts of sulfonated phenol-formaldehyde condensates; or more complex sulfonates such as the amide sulfonates, e.g. the sulfonated condensation product of oleic acid and N-methyl taurine or the dialkyl sulfosuccinates, e.g. the sodium sulfonate of dioctyl succinate. Nonionic agents include condensation products of fatty acid esters, fatty alcohols, fatty acid amides or fatty-alkyl- or alkenyl-substituted phenols with ethylene oxide, fatty esters of polyhydric alcohol ethers, e.g. sorbitan fatty acid esters, condensation products of such esters with ethylene oxide, e.g. polyoxyethylene sorbitan fatty acid esters, block copolymers of ethylene oxide and propylene oxide, acetylenic glycols such as 2,4,7,9-tetramethyl-5-decyne-4,7-diol, or ethoxylated acetylenic glycols.

Examples of a cationic surface-active agent include, for instance, an aliphatic mono-, di-, or polyamine as an acetate, naphthenate or oleate; an

oxygen-containing amine such as an amine oxide or polyoxyethylene alkylamine; an amide-linked amine prepared by the condensation of a carboxylic acid with a di- or polyamine; or a quaternary ammonium salt.

The compositions of the invention can take any form known in the art for the formulation of agrochemicals, for example, a solution, a dispersion, an aqueous emulsion, a dusting powder, a seed dressing, a fumigant, a smoke, a dispersible powder, an emulsifiable concentrate or granules. Moreover it can be in a suitable form for direct application or as a concentrate or primary composition which requires dilution with a suitable quantity of water or other diluent before application.

An emulsifiable concentrate comprises a compound of the invention dissolved in a water-immiscible solvent which is formed into an emulsion with water in the presence of an emulsifying agent.

A dusting powder comprises a compound of the invention intimately mixed and ground with a solid pulverulent diluent, for example, kaolin.

A granular solid comprises a compound of the invention associated with similar diluents to those which may be employed in dusting powders, but the mixture is granulated by known methods. Alternatively it comprises the active ingredient absorbed or adsorbed on a pre-granular diluent, for example, Fuller's earth, attapulgite or limestone grit.

Wettable powders, granules or grains usually comprise the active ingredient in admixture with a suitable surfactant and an inert powder diluent such as china clay.

Another suitable concentrate is a flowable suspension concentrate which is formed by grinding the compound with water or other liquid, a wetting agent and a suspending agent.

The concentration of the active ingredient in the composition of the present invention, as applied to plants is preferably within the range of 0.0001 to 1.0 %

(w/w), especially 0.0001 to 0.01 % (w/w). In a primary composition, the amount of active ingredient can vary widely and can be, for example, from 5 to 95 % (w/w) of the composition.

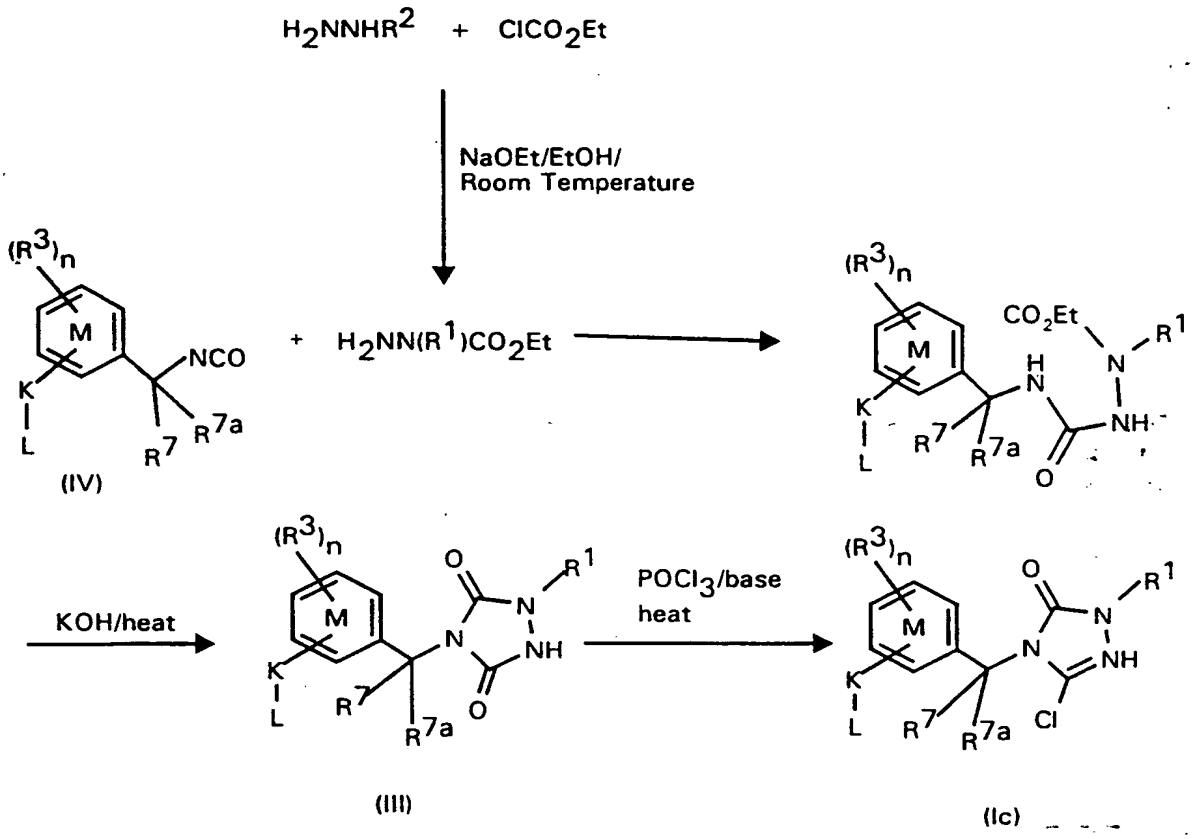
In the method of the invention the compound is generally applied to seeds, plants or their habitat. Thus, the compound can be applied directly to the soil before, at or after drilling so that the presence of active compound in the soil can control the growth of fungi which may attack seeds. When the soil is treated directly the active compound can be applied in any manner which allows it to be intimately mixed with the soil such as by spraying, by broadcasting a solid form of granules, or by applying the active ingredient at the same time as drilling by inserting it in the same drill as the seeds. A suitable application rate is within the range of from 5 to 1000 g per hectare, more preferably from 10 to 500 g per hectare.

Alternatively the active compound can be applied directly to the plant by, for example, spraying or dusting either at the time when the fungus has begun to appear on the plant or before the appearance of fungus as a protective measure. In both such cases the preferred mode of application is by foliar spraying. It is generally important to obtain good control of fungi in the early stages of plant growth as this is the time when the plant can be most severely damaged. The spray or dust can conveniently contain a pre- or post-emergence herbicide if this is thought necessary. Sometimes, it is practicable to treat the roots of a plant before or during planting, for example, by dipping the roots in a suitable liquid or solid composition. When the active compound is applied directly to the plant a suitable rate of application is from 0.025 to 5 kg per hectare, preferably from 0.05 to 1 kg per hectare.

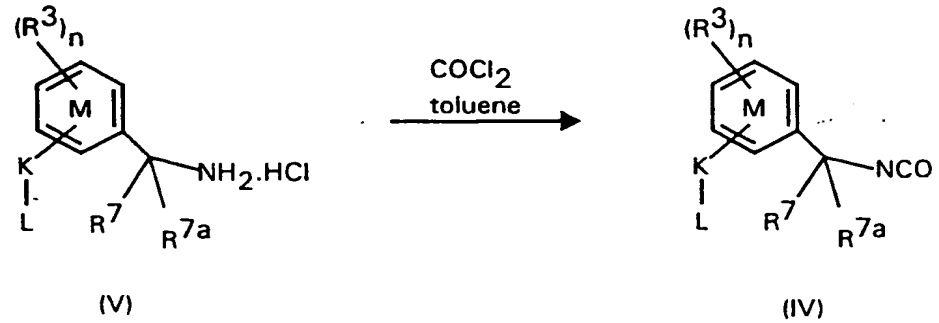
Compounds of the invention may be prepared, in known manner, in a variety of ways.

Compounds of formula Ic, i.e. compounds of general formula I where R^2 is chlorine, can be prepared from isocyanate IV as shown in the following reaction sequence. Analogous compound to Ic, where R^2 in compound I is a different

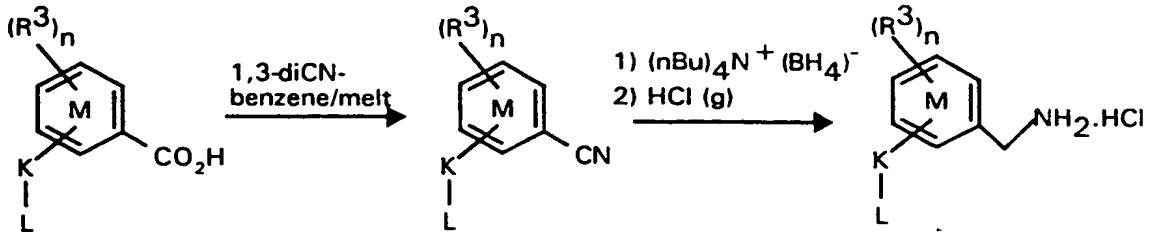
halogen, can be prepared using this reaction sequence by adopting alternative halogenation methodology.



The starting isocyanates IV can prepared in one stage by reacting the corresponding primary amine hydrochloride V with phosgene.

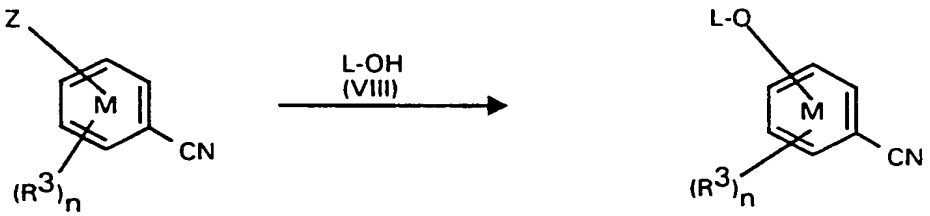


Primary amine hydrochloride Va, i.e. where R^7 and R^{7a} are hydrogen in V, may be prepared according to the following reaction sequence via cyano intermediate VI.



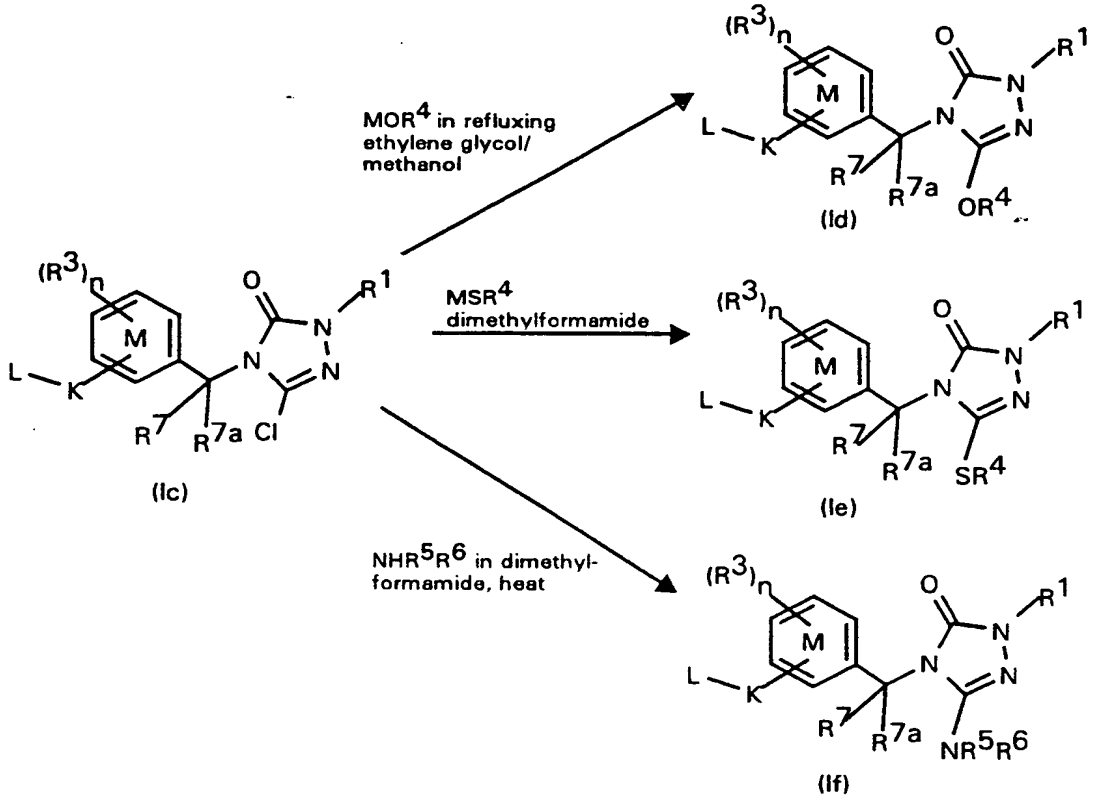
(VI) (Va)

Cyano intermediate VIa, i.e. general intermediate VI where K is -O-, may be prepared by coupling compound VII, where Z is a leaving group for example halogen, with an hydroxy compound VIII. In the case when VIII is a phenol, the reaction conditions are preferably copper in refluxing ethanol. The skilled person will realise that, in appropriate cases, modification of the group -K-L may be performed after construction of the triazole ring.

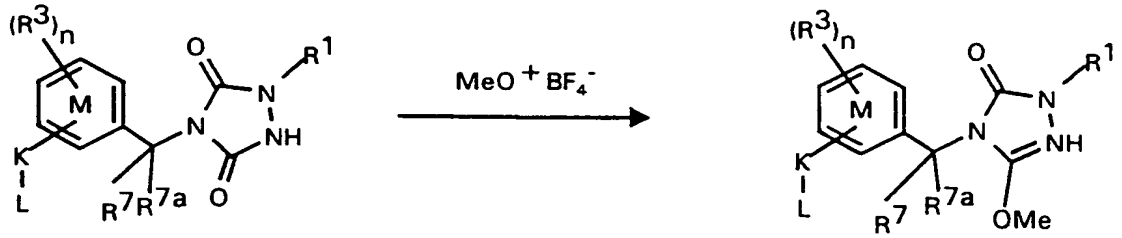


(VII) (VIa)

Compounds of formula Ic can be converted into further compounds of general formula I. For example, compounds of formula Id where R^2 is $-OR^4$ can be prepared by reacting Ic with a compounds of formula $M^{+-}OR^4$, where M is a metal. Similarly, compounds of formula Ie where R^2 is $-SR^4$ can be prepared by reacting Ic with compounds of formula $M^{+-}SR^4$. Compounds of formula If where R^2 is NR^5R^6 can be prepared by reacting Ic with a corresponding primary or secondary amine, NHR^5R^6.

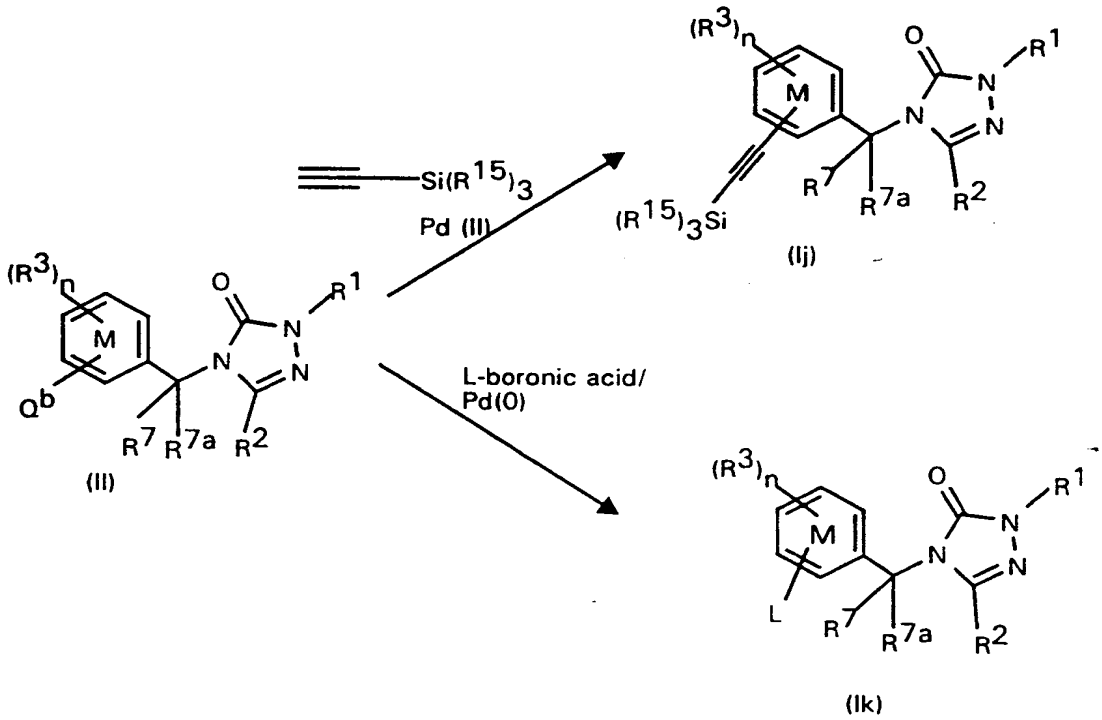


Alternatively compounds of formula Id, where R^4 is methyl can be prepared in a single step from intermediate III by treatment with trimethyl oxonium tetrafluoroborate, according to the following reaction sequence.



Modification of the group -K-L can be performed using a number of transformations known to the skilled person, either before or after construction of the five membered heterocycle. For example compounds of formula Ij, i.e. compounds of formula I where K is -C≡C- and L is $-Si(R^{15})_3$, can be prepared by palladium coupling of compound II, where Q^b is preferably a halogen, especially bromine or iodine, with $HC{\equiv}CSi(R^{15})_3$. Similarly, compounds of formula Ik, i.e.

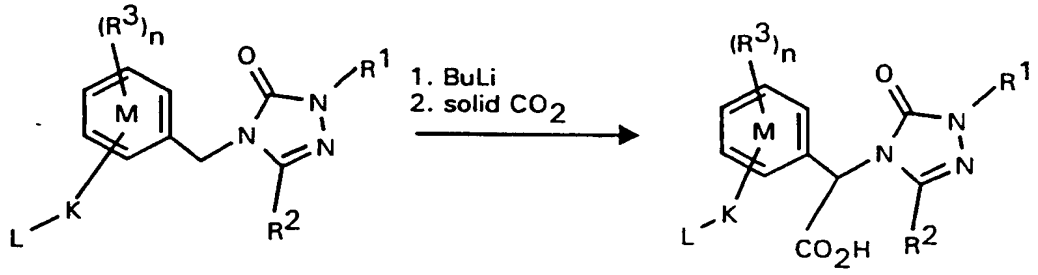
compounds of formula I where K is a direct bond and L is an aromatic carbocyclyl or heterocyclyl group, can be prepared by coupling II with a suitable boronic acid derivative.



(II) (Ij) (Ik)

Compounds of formula II can be prepared according to the chemistry described hereinabove starting from the corresponding analogue of amine hydrochoride V.

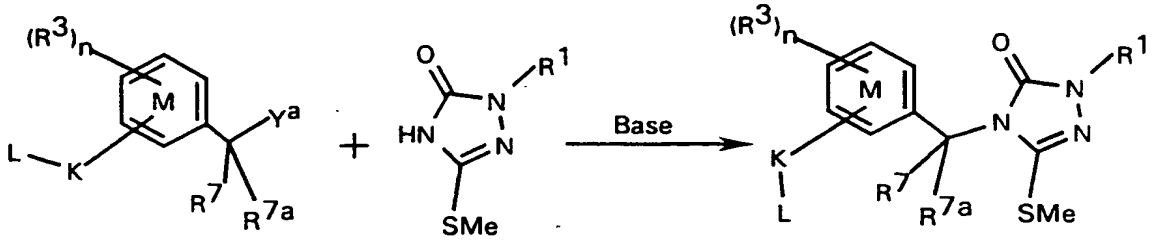
Compounds of formula Im, i.e. compounds of general formula I where R^7 is carboxy and R^{7a} is hydrogen, can be prepared according to the following reaction sequence from compounds of formula In where R^7 and R^{7a} are hydrogen in I.



(In) (Im)

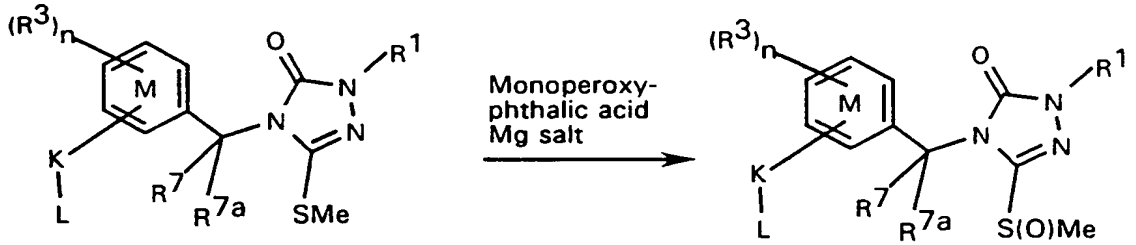
Alternatively compounds of formula Ip, i.e compounds of general formula I where R^2 is SMe, may be prepared according to the following reaction scheme. Typical

reaction conditions comprise treating compounds X with a base, such as sodium hydride, followed by addition of XI, where Y^a is a leaving group such as halogen.

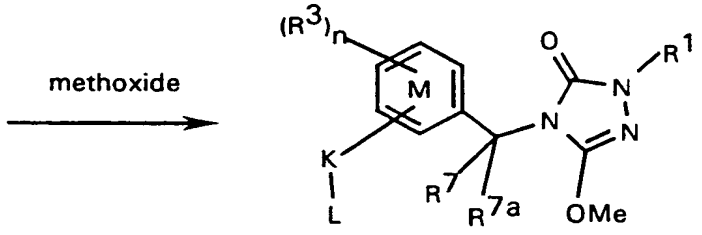


(XI) (X) (Ip)

Compounds of formula Iq where R^2 is S(O)Me can be prepared from compounds of formula Ip by treatment with a compound such as monoperoxyphthalic acid magnesium salt hexahydrate in the presence of benzyltriethylammonium chloride. Compounds of formula Ir where R^2 is OMe can be prepared in turn from compounds of formula Iq by treatment with a methoxide source, such as sodium methoxide in methanol.



(Ip) (Iq)



(Ir)

In those cases where the group -K-L is unstable to methoxide, the methoxy group was introduced prior to construction of K-L.

Other methods will be apparent to the chemist skilled in the art as will be the methods for preparing starting materials and intermediates.

The following Examples also make apparent various methods of preparing compounds of the invention as well as starting materials and intermediates of the invention. Structures of isolated novel compounds were confirmed by elemental and/or other appropriate analyses.

Example 1

3-Methoxy-1-methyl-4-{4-[2-(1,1,1-trimethylsilyl)ethynyl]benzyl}-4,5-dihydro-1*H*-1,2,4-triazol-5-one (Compound 1a)

A solution of 4-(3-bromobenzyl)-3-methoxy-4,5-dihydro-1*H*-1,2,4-triazol-5-one (500 mg, the product from stage (d) below), trimethylsilylacetylene (267 mg), palladium (II) acetate (18.8 mg), triphenyl phosphine (36.7 mg) in dry triethylamine (1.45 ml) and toluene (1.5 ml) was heated under reflux for 3 hours. The solution was cooled, filtered and the residue washed with toluene. The filtrate and washings were combined and the solvent was removed. The residue was purified by silica gel chromatography to give the title compound, ^{1}H N.M.R. ($CDCl_3$) δ 0.12, (9H, s, $SiMe_3$); 3.29 (3H, s, NMe); 3.95 (3H, s, OMe); 4.63 (2H, s, NCH_2Ar) and 7.2-7.43 (4H, m, Ar).

Preparation of Starting Material

a) 3-Bromobenzyl isocyanate

Phosgene was bubbled through a suspension of 3-bromobenzylamine hydrochloride (5.0 g) in refluxing toluene (270 ml) for 2.5 hours. After cooling to room temperature, the solvent was evaporated to give the title compound which was used in stage b) without further purification.

b) Ethyl 2-{[(3-bromobenzyl)amino]carbonyl}-1-methylhydrazine-1-carboxylate

To a solution of 3-bromobenzyl isocyanate (1.0 g) in dichloromethane (20 ml) cooled to 10 °C was added a solution of ethyl 1-methylhydrazino-

carboxylate (0.56 g) in dichloromethane (10 ml) over a period of 5 minutes. After addition, the reaction mixture was allowed to warm to room temperature over 2 hours. Removal of the solvent gave the title compound as an oil which was used in stage c) without further purification.

c) 4-(3-Bromobenzyl)-1-methyl-1,2,4-triazolidin-3,5-dione

A solution of the product from stage b) (0.95 g) in aqueous potassium hydroxide (10 ml, 2M) was heated under reflux for 45 minutes. After cooling, the solution was acidified to pH 1 with concentrated hydrochloric acid solution, and extracted with dichloromethane. The organic extracts were combined and dried ($MgSO_4$), and evaporated to give the title compound as a solid, m.p. 109-113 °C.

d) 4-(3-Bromobenzyl)-1-methyl-3-methoxy-4,5-dihydro-1*H*-1,2,4-triazol-5-one

A solution of the product from stage c) (2.25 g) and trimethyloxoniumtetrafluoro-borate (4.03 g) in dichloromethane (119 ml) was heated under reflux for 2.5 hours. After cooling the reaction mixture was washed successively with saturated aqueous sodium bicarbonate (100 ml), then water (100 ml) and finally brine (100 ml), followed by drying ($MgSO_4$) and evaporation to give a the title compound as a solid, m.p. 79-82 °C.

Example 2

3-Methoxy-1-methyl-4-[(1,1':4',1"-terphenyl-3-yl)methyl]-4,5-dihydro-1*H*-1,2,4-triazol-5-one (Compound 2a)

A solution of 4-(3-bromobenzyl)-3-methoxy-1-4,5-dihydro-1*H*-1,2,4-triazol-5-one (1.3 g, the product from stage (d) above), 4-phenylbenzeneboronic acid (1.1 g), tetrakistriphenylphosphine palladium (0) (0.25 g) in toluene (12 ml), ethanol (3.5 ml) and aqueous sodium carbonate (5.9 ml, 2M) were heated under reflux for 18 hours. The reaction mixture was allowed to cool and then washed with brine (2 x 20 ml). The aqueous layers were combined and then extracted with toluene (50 ml). All organic phases were combined, dried ($MgSO_4$), and the solvent removed. The residue was purified by silica gel column chromatography to give the title

compound, ^{1}H N.M.R. ($CDCl_3$) δ 3.2 (3H, s, NMe); 3.95 (3H, s, OMe); 4.68 (2H, s NCH_2Ar) and 7.2-7.65 (13H, m, Ar).

Example 3

4-(α-Carboxybenzyl)-3-methoxy-1-methyl-4,5-dihydro-1*H*-1,2,4-triazol-5-one (Compound 1c)

To a solution of 4-(2-bromobenzyl)-3-methoxy-1-methyl-4,5-dihydro-1*H*-1,2,4-triazol-5-one (0.5 g) in tetrahydrofuran (5 ml) at -78 °C was added butyllithium (0.67 ml, 2.5 M in hexane) and the solution stirred at -78 °C for 1 hour. The reaction mixture was poured onto solid carbon dioxide and stirred for 45 mins. Aqueous potassium bicarbonate (30 ml) was then added and the solution was stirred for 10 minutes at room temperature. The solution was acidified with concentrated hydrochloric acid and the solution was extracted with diethyl ether (2x30 ml). The combined organic phases were washed with brine, dried ($MgSO_4$), filtered and the solvent removed to give the title compound, m.p.170-172°C.

Preparation of starting material

4-(2-Bromobenzyl)-3-methoxy-1-methyl-4,5-dihydro-1*H*-1,2,4-triazol-5-one was prepared in analogous fashion to Example 1 [see stages a) to d)] using 2-bromobenzylamine hydrochloride in stage a).

Example 4

4-[2-Chloro-5-(*N*-3-trifluorormethylphenyl-*S*-methylisodithiocarbamoyl-methyl)benzyl]-3-methoxy-1-methyl-4,5-dihydro-1*H*-1,2,4-triazol-5-one (compound 29b)

Sodium hydride (0.08 g, 60% in oil) was added portionwise to a stirred solution of methyl 3-trifluorormethylphenyl-*S*-methylisodithiocarbamate (0.48 g) in tetrahydrofuran (10 ml) and dry dimethylformamide (5 ml) at 5°C. The product from stage a) (0.5 g) in tetrahydrofuran (15 ml) was added at 5 °C and the reaction mixture was stirred at room temperature for 48 hours. Isopropyl alcohol (4 drops) was added and the reaction mixture was added to ice/water. The mixture was extracted with diethyl ether (x3). The combined ether extracts were washed with water, dried ($MgSO_4$), filtered and the solvent removed. The residue

was purified by silica gel chromatography eluting with diethyl ether/dichloromethane (1:1) to give the title product as an oil.

Preparation of Starting Materials

a) 4-[(2-Chloro-5-chloromethyl)benzyl]-3-methoxy-1-methyl-4,5-dihydro-1*H*-1,2,4-triazol-5-one.

To an ice-cooled solution of the product from stage b) (1.25 g) and diisopropylethylamine (1.0 g) in dry tetrahydrofuran (30 ml) was added a solution of methanesulfonyl chloride (0.6 g) in dry tetrahydrofuran (5 ml) and stirring was continued at 5°C for 5 minutes and at room temperature for 24 hours. The reaction mixture was evaporated to dryness, the residue dissolved in diethyl ether and washed with water (x2). The organic phase was dried ($MgSO_4$), filtered and the solvent removed. The residue was washed with petrol to give the title product as a solid, m.p.112-4 °C.

b) 4-[(2-Chloro-5-hydroxymethyl)benzyl]-3-methoxy-1-methyl-4,5-dihydro-1*H*-1,2,4-triazol-5-one.

To a solution of the product from stage c) (1.88 g) in *tert*-butanol (28 ml) was added sodium borohydride (0.57 g). The reaction mixture was heated to reflux and methanol (5.6 ml) added over 1.25 hours. The reaction mixture was heated under reflux for a further 2.5 hours. On cooling, ethyl acetate was added and the reaction mixture was washed with water. The aqueous extracts were extracted with ethyl acetate and the combined ethyl acetate extracts were washed with water, dried ($MgSO_4$), filtered and the solvent removed to give a residue which was washed with diisopropyl ether to give the title product, m.p. 119-21 °C.

c) 4-[(2-Chloro-5-methoxycarbonyl)benzyl]-3-methoxy-1-methyl-4,5-dihydro-1*H*-1,2,4-triazol-5-one.

To an ice-cooled solution of the product from stage d) (11.8 g) in methanol (80 ml) was added sodium methoxide (9.3 g) in methanol (60 ml). The reaction mixture was allowed to warm to room temperature and stirred for 18 hours. Diethyl ether was added and the mixture was washed with water. The aqueous phase was re-extracted with diethyl ether and the

combined organic extracts were washed with water, dried $MgSO_4$ and the solvent removed to give the title product as a solid, m.p. 129-30 °C.

d) 4-[(2-Chloro-5-methoxycarbonyl)benzyl]-3-methylsulfinyl-1-methyl-4,5-dihydro-1*H*-1,2,4-triazol-5-one.

To an ice-cooled, stirred solution of the product from stage e) (11.2 g) in dichloromethane (120 ml) was added monoperoxyphthalic acid magnesium salt hexahydrate (15.9 g) in water (100 ml). The reaction mixture was stirred for 1.5 hours at 5 °C and 3.5 hours at room temperature. The layers were separated and the aqueous phase was extracted with dichloromethane (x2). The combined organic extracts were washed with water, dried ($MgSO_4$), filtered and the solvent removed to give the title product which was used in stage c) without further purification.

e) 4-[(2-Chloro-5-methoxycarbonyl)benzyl]-3-methylthio-1-methyl-4,5-dihydro-1*H*-1,2,4-triazol-5-one.

To an ice-cooled solution of the product from stage f) (11.2 g) in dry tetrahydrofuran (20 ml) was added sodium hydride (3.2 g, 60% in oil) portion-wise. After 10 minutes, methyl 3-bromomethyl-4-chlorobenzoate (20 g) in dry dimethylformamide (80 ml) was added, stirred at 5°C for 1 hour and then at room temperature for 3 hours. Isopropyl alcohol (4 drops) was added, followed by ice/water. The reaction mixture was extracted with diethyl ether (x3), dried ($MgSO_4$) and the solvent removed to give the title product as a solid, m.p. 136-8 °C.

f) 1-Methyl-3-methylthio-4,5-dihydro-1*H*-1,2,4-triazol-5-one.

To a stirred solution of ethyl 1-methylhydrazinocarboxylate (23.6 g) and potassium thiocyanate (19.4 g) in ethanol (150 ml) at 5 °C was added concentrated hydrochloric acid (20 ml). The reaction mixture was allowed to warm to room temperature over 1.5 hours, and then heated under reflux for 1.5 hours. The mixture was evaporated to dryness, and water was added. The mixture was stirred with ice-cooling and then filtered. The resulting solid was added to a solution of sodium hydroxide (10.2 g) in water (70 ml) and the solution was heated under reflux for 1 hour. The

mixture was cooled in ice and benzytriethylammonium chloride (3 mg) was added followed by methyl iodide (18.1 g) in dichloromethane (30 ml). The reaction mixture was stirred at room temperature for 22 hours. The mixture was cooled in ice and acidified with hydrochloric acid. The pH was then adjusted to approx. pH 4 with saturated aqueous sodium bicarbonate, and the mixture was filtered. The resulting solid was washed with water, then with ether and dried to give the title product.

Example 5

4-{[2-Chloro-5-(3-trifluoromethyl)acetophenoneoximinomethyl]benzyl}-3-methylthio-1-methyl-4,5-dihydro-1*H*-1,2,4-triazol-5-one (compound 62b)

To a stirred, ice-cooled solution of 3-trifluoromethylacetophenone oxime (0.6 g) in dry dimethylformamide (10 ml) was added potassium *tert*-butoxide (0.35 g) and stirring continued for 5 minutes. The product from stage a) (0.9 g) in dry dimethylformamide (10 ml) was then added and the mixture was stirred at room temperature for 6 hours. Diethyl ether was added and the mixture was washed with water (x3). The organic phase was dried ($MgSO_4$), filtered and the solvent removed. The residue was purified by silica gel chromatography eluting with diethyl ether/ dichloromethane to give the title product, m.p. 117-9 °C.

Preparation of Starting Materials

a) 4-[(2-Chloro-5-chloromethyl)benzyl]-3-methylthio-1-methyl-4,5-dihydro-1*H*-1,2,4-triazol-5-one.

This compound was obtained from the product of stage b) below using analogous methodology to Example 4 stage a).

b) 4-[(2-Chloro-5-hydroxymethyl)benzyl]-3-methylthio-1-methyl-4,5-dihydro-1*H*-1,2,4-triazol-5-one.

This compound was obtained from the product of Example 4 stage e) using analogous methodology to Example 4 stage b).

Example 6

4-{[2-Chloro-5-(3-trifluoromethyl)acetophenoneoximinomethyl]benzyl}-3-methoxy-1-methyl-4,5-dihydro-1*H*-1,2,4-triazol-5-one (compound 28b)

This compound was obtained from the product of stage a) below using analogous methodology to Example 4 stage c).

Preparation of Starting Materials

a) 4-{[2-Chloro-5-(3-trifluoromethyl)acetophenoneoximinomethyl]benzyl}-3-methylsulfinyl-1-methyl-4,5-dihydro-1*H*-1,2,4-triazol-5-one

This compound was obtained from the product of Example 5 using analogous methodology to Example 4 stage d).

Example 7

4-{3-[(2-Methylphenoxy)methyl]benzyl}-3-methoxy-1-methyl-4,5-dihydro-1*H*-1,2,4-triazol-5-one (Compound 22a)

This compound was obtained from the product of stage a) below using analogous methodology to Example 4 stage c).

Preparation of Starting Materials

a) 4-{3-[(2-Methylphenoxy)methyl]benzyl}-3-methylsulfinyl-1-methyl-4,5-dihydro-1*H*-1,2,4-triazol-5-one

This compound was obtained from the product of stage b) below using analogous methodology to Example 4 stage d).

b) 4-{3-[(2-Methylphenoxy)methyl]benzyl}-3-methylthio-1-methyl-4,5-dihydro-1*H*-1,2,4-triazol-5-one

This compound was obtained from the product of stage c) below and 2-methylphenol using analogous methodology to Example 5.

c) 4-(3-Bromomethylbenzyl)-3-methylthio-1-methyl-4,5-dihydro-1*H*-1,2,4-triazol-5-one

This compound was obtained from the product of Example 4 stage f) and α,α'-dibromo-*m*-xylene using analogous methodology to Example 4 stage e).

Example 8

Compound 28a

The compound was obtained from the product of stage a) below and methyl 2-[(3-trifluoromethylbenzylidene]hydrazinocarbodithioate using analogous methodology to Example 4.

Preparation of Starting Materials

a) 4-(3-Chloromethylbenzyl)-3-methoxy-1-methyl-4,5-dihydro-1*H*-1,2,4-triazol-5-one

This compound was obtained from the product of stage b) below using analogous methodology to Example 4 stage a).

b) 4-(3-Hydroxymethylbenzyl)-3-methoxy-1-methyl-4,5-dihydro-1*H*-1,2,4-triazol-5-one

This compound was obtained from the product of stage c) below using analogous methodology to Example 4 stage c).

c) 4-(3-Acetoxymethylbenzyl)-3-methylsulfinyl-1-methyl-4,5-dihydro-1*H*-1,2,4-triazol-5-one

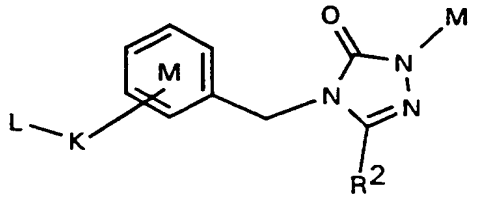
This compound was obtained from the product of stage d) below using analogous methodology to Example 4 stage d).

d) 4-(3-Acetoxymethylbenzyl)-3-methylthio-1-methyl-4,5-dihydro-1*H*-1,2,4-triazol-5-one

A mixture of the product from Example 7, stage c) (2.0 g) and potassium acetate (1.2 g) in dry acetonitrile (20 ml) was heated under reflux for 3 hours. On cooling, diethyl ether was added and the mixture was washed

with water (x2), The organic layer was dried ($MgSO_4$) and the solvent removed to give the title product.

The compounds of formula Ix, i.e. compounds of general formula I where R^1 is Me, R^7 and R^{7a} are hydrogen and n is 0 (see Table A) were prepared by methods analogous to those of the above Examples. The column headed "Position" contains the position of the substituent -K-L on the benzene ring M.

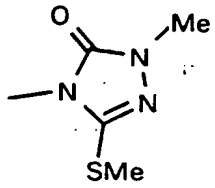
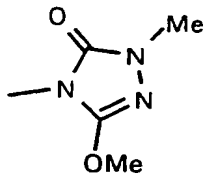


Iz

Table A

Cmp	Pos	R^2	K	L	m.p./°C
3a	3	OMe	direct bond	2-thienyl	oil
4a	3	OMe	direct bond	4-Cl-phenyl	oil
5a	3	OMe	direct bond	3,5-diCl-phenyl	125-29
6a	3	OMe	-C≡C-	$C(OH)Me_2$	oil
7a	3	OMe	-C≡C-	*tert*-butyl	oil
8a	2	OMe	direct bond	4-biphenylyl	oil
9a	2	OMe	direct bond	3,5-diCl-phenyl	oil
10a	2	OMe	-C≡C-	trimethylsilyl	oil
11a	2	OMe	direct bond	4-Cl-phenyl	oil
12a	3	OMe	direct bond	4-biphenylyl	oil
13a	3	OMe	-C≡C-	phenyl	oil
14a	2	OMe	-C≡C-	phenyl	98-102
15a	2	OMe	direct bond	2-thienyl	100-7
16a	2	OMe	-C≡C-	$C(OMe)Me_2$	oil
17a	2	OMe	-C≡C-	*tert*-butyl	68-71
18a	2	OMe	-C≡C-	$C(OH)Me_2$	oil
19a	4	OMe	-O-	4-Cl-phenyl	oil
20a	2	OMe	$-CH_2O-$	3,4-diMeO-benzyl	oil

Cmp	Pos	R^2	K	L	m.p./°C
21a	3	OMe	$-CH_2O-N=C(Me)-$	3-CF_3-phenyl	oil
22a	3	OMe	$-CH_2O-$	2-tolyl	oil
23a	3	OMe	$-CH_2SC(SMe)=N-$	3-CF_3-phenyl	oil
24a	3	OMe	$-CH_2O-N=C(Me)-$	5-indanyl	oil
25a	3	OMe	$-CH_2SC(SMe)=N-$	4-tolyl	oil
26a	3	OMe	$-CH_2SC(SMe)=N-$	4-Br-phenyl	oil
28a	3	OMe	$-CH_2SC(SMe)=N-N=CH-$	3-CF_3-phenyl	oil
29a	3	OMe	-O-	3-(3-Br-phenyl)-1,2,4-thiadiazol-5-yl	152-3
30a	3	OMe	-O-	3-(3,5-diCF_3-phenyl)-1,2,4-thiadiazol-5-yl	98-99
31a	3	OMe	-O-	3-(3,4-diCl-phenyl)-1,2,4-thiadiazol-5-yl	138-40
32a	3	OMe	$-CH_2OC(Me)=N-N=C(Me)-$	4-Cl-phenyl	oil
33a	3	OMe	$-CH_2N$(acetyl)$-N=C(Me)--$	4-Cl-phenyl	oil
34a	2	OMe	$-CH_2O-N=C(Me)-$	3-CF_3-phenyl	oil
35a	2	OMe	$-CH_2O-$	2-tolyl	73-5
36a	4	OMe	-O-	Me	81-5
37a	4	OMe	$-OCH_2-$	phenyl	84-8
38a	2	OMe	$-CH_2S-C(SMe)=N-$	3-CF_3-phenyl	oil
39a	2	OMe	$-CH_2S-C(SMe)=N-N=CH-$	4-Cl-phenyl	55-63
40a	3	Cl	$-CH_2O-N=C(Me)-$	3-CF_3-phenyl	oil
41a	3	Cl	-O-	Me	oil
42a	3	SMe	direct bond	$-CH_2Br$	87-9
43a	3	SMe	$-CH_2O-$	2-tolyl	oil
44a	3	SMe	direct bond	$-CH_2OC(=O)Me$	oil
45a	3	S(O)Me	direct bond	$-CH_2OC(=O)Me$	oil

Cmp	Pos	R^2	K	L	m.p./°C
46a	2	SMe	direct bond	$-CH_2Br$	128-30
47a	2	SMe	$-CH_2-$		184-6
48a	2	SMe	$-CH_2O-N=C(Me)-$	3-CF_3-phenyl	89-91
49a	2	SMe	$-CH_2O-$	2-tolyl	oil
50a	4	SMe	$-OCH_2-$	phenyl	80-2
51a	4	S(O)Me	$-OCH_2-$	phenyl	oil
52a	4	$S(O)_2Me$	$-OCH_2-$	phenyl	oil
53a	2	SMe	direct bond		oil
54a	4	SMe	-O-	Me	120-2

Some of those compounds in the Table A which do not have discrete melting points have the following characteristic ^1H N.M.R. data in $CDCl_3$.

Compound 3a δ 3.37 (3H, s, NMe); 3.93 (3H, s, OMe); 4.68 (2H, s, NCH_2Ar) and 7.10-7.7 (7H, m, Ar).

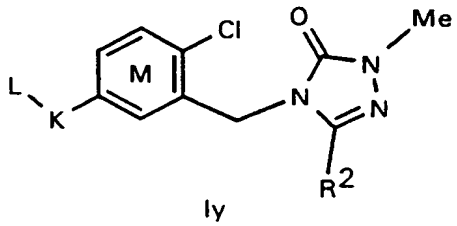
Compound 4a δ 3.37 (3H, s, NMe); 3.92 (3H, s, OMe); 4.78 (2H, s, NCH_2Ar) and 7.22-7.8 (8H, m, Ar).

Compound 5a δ 3.37 (3H, s, NMe); 3.93 (3H, s, OMe); 4.75 (2H, s, NCH_2Ar) and 7.23-7.6 (7H, m, Ar).

Compound 6a δ 1.6 (6H, s, CMeOH), 3.4 (3H, s, NMe); 3.90 (3H, s, OMe); 4.63 (2H, s NCH_2Ar) and 7.20-7.70 (4H, m, Ar).

Compound 7a δ 1.13 (9H, s, $C(Me)_3$), 3.4 (3H, s, NMe); 3.9 (3H, s, OMe); 4.6 (2H, s NCH_2Ar) and 7.15-7.37 (4H, m, Ar).

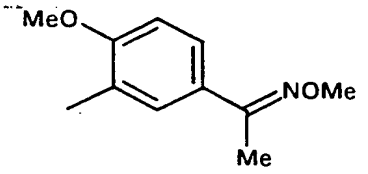
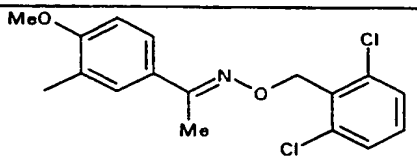
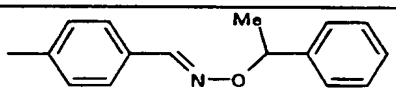
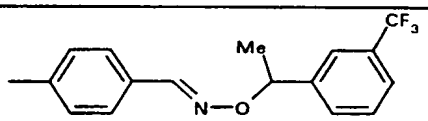
The following compounds of formula Iy, i.e. compounds of general formula I where R^1 is Me, R^7 and R^{7a} are hydrogen, n is 1, R^3 is Cl positioned at the 2 position of benzene ring M, and –K-L is positioned at the 5 position of benzene ring M (see Table B), were also prepared by methods analogous to those of the above Examples.

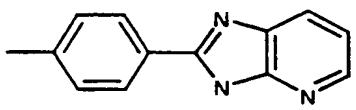
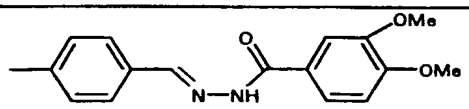
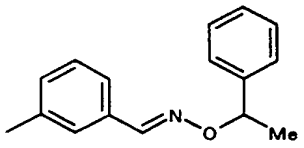
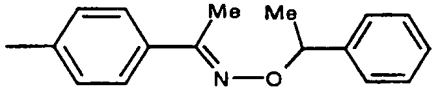
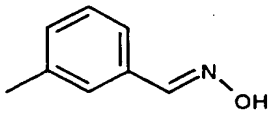
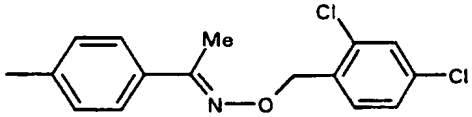
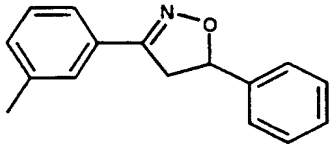
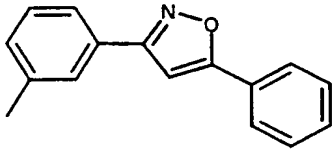


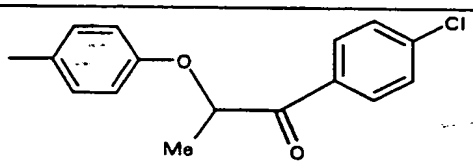
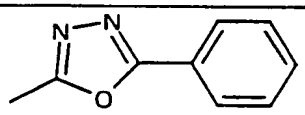
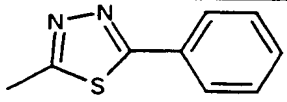
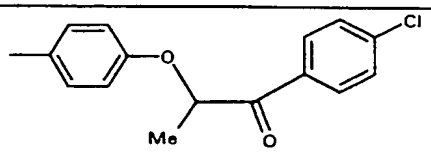
Iy

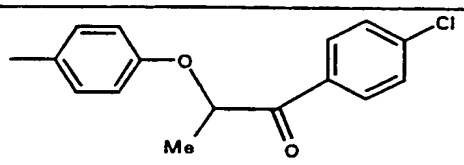
Table B

Cmd	R^2	K	L	m.p. /°C
1b	OMe	direct bond	2-thienyl	93-4
2b	OMe	direct bond	3,5-diCl-phenyl	149-50
3b	OMe	direct bond	4-Cl-phenyl	131-3
4b	OMe	-C≡C-	trimethylsilyl	146-7
5b	OMe	-C≡C-	$C(OH)Me_2$	135-6
6b	OMe	direct bond	biphenylyl	167-8
7b	OMe	-C≡C-	phenyl	155-7
8b	OMe	-C≡C-	tert-butyl	119-21
9b	OMe	-C≡C-	$C(OMe)Me_2$	102-3
10b	OMe	-O-	3-(3,4-diCl-phenyl)-1,2,4-thiadiazol-5-yl	134-6
11b	OMe	-O-	3-(3,5-diCF_3-phenyl)-1,2,4-thiadiazol-5-yl	125-7
12b	OMe	-O-	3-phenyl-1,2,4-thiadiazol-5-yl	130-2
13b	OMe	-O-	phenylethyl	oil
14b	OMe	$-OCH_2-$	2,5-xylyl	98-9

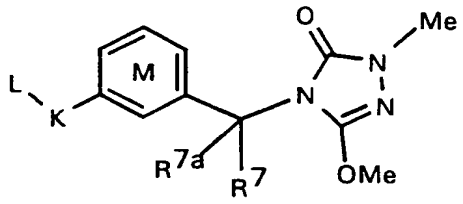
Cmd	R^2	K	L	m.p. /°C
15b	OMe	$-OCH_2-$	2-Cl-phenyl	oil
16b	OMe	$-OCH_2-$	2-CN-phenyl	136-7
17b	OMe	-O-	2,4,6-triCl-phenoxyethyl	146-7
18b	OMe	$-OCH_2-$	2-MeO-5-acetyl-phenyl	157-9
19b	OMe	-O-	3-Cl-5-CF_3-2-pyridyl	139-40
20b	OMe	$-OCH_2-$	2-Cl-3-(propargyloxy)-phenyl	113-4
21b	OMe	$-OCH_2-$		136-8
22b	OMe	$-OCH_2-$		123-4
23b	OMe	direct bond	4-formyl-phenyl	150-2
24b	OMe	direct bond		115-6
25b	OMe	direct bond		118-9
26b	OMe	-O-	4,6-diMeO-pyrimidin-2-yl	162-4
27b	OMe	direct bond	2-benzo[b]furanyl	147-8
28b	OMe	$-CH_2O-N=C(Me)-$	3-CF_3-phenyl	100-2
29b	OMe	$-CH_2SC(SMe)=N-$	3-CF_3-phenyl	
30b	OMe	$-CH_2SC(SMe)=N-$	4-Br-phenyl	70-4
31b	OMe	$-CH_2O-$	2-tolyl	130-2
32b	OMe	$-CH_2O-N=C(Me)-$	5-indanyl	106-8
33b	OMe	$-CH_2OC(Me)=N-$ $N=C(Me)-$	4-Cl-phenyl	114-22
34b	OMe	$-CH_2N$(acetyl)- $N=C(Me)-$	4-Cl-phenyl	125-7
35b	OMe	direct bond	4-carboxyphenyl	240-50

Cmd	R^2	K	L	m.p. /°C
36b	OMe	direct bond		203-5
37b	OMe	direct bond		193-4
38b	OMe	direct bond	3-formyl-phenyl	120-2
39b	OMe	-C(=O)NH-	3,3-diphenylpropyl	109-10
40b	OMe	direct bond	1,3-isoxazol-5-yl	137-9
41b	OMe	direct bond		oil
42b	OMe	direct bond	4-(hydroxyethyl)phenyl	156-8
43b	OMe	direct bond	4-acetylphenyl	160-1
44b	OMe	direct bond		oil
45b	OMe	direct bond	3-(2,2-dicyanovinyl)phenyl	162-4
46b	OMe	direct bond		136-8
47b	OMe	direct bond		129-32
48b	OMe	direct bond		oil
49b	OMe	direct bond		176-9
50b	OMe	direct bond	4-(hydroxymethyl)-phenyl	140-2
51b	OMe	direct bond	4-MeO-phenyl	113-26
52b	OMe	direct bond	5-phenyl-1,3,4-oxadiazol-2-yl	165-7

Cmd	R^2	K	L	m.p. /°C
53b	OMe	-C(=O)NH-	3-Cl-5-CF_3-2-pyridylmethyl	164-5
54b	OMe	direct bond	4-(4-Cl-benzyloxy)phenyl	176-88
55b	OMe	direct bond		142-9
56b	OMe	direct bond	4-(2-CN-phenoxy)phenyl	108-11
57b	OMe	-C(=O)NH-	4-Cl-phenyl-2-ethyl	153-4
58b	SMe	-O-	Me	94-5
59b	SMe	direct bond	$-CH_2OH$	120-2
60b	OMe	-O-	$-CH(Me)C(OMe)=CHCO_2Me$	oil
61b	SMe	direct bond	$-CH_2Cl$	117-9
62b	SMe	$-CH_2ON=C(Me)-$	3-CF_3-phenyl	117-9
63b	SMe	$-CH_2O-$	2-tolyl	105-7
64b	OMe	direct bond	$-CH_2OH$	119-121
65b	OMe	direct bond	$-CH_2Cl$	112-4
66b	SMe	direct bond	4-MeO-phenyl	119-121
67b	SMe	direct bond	4-HO-phenyl	224-6
68b	S(O)Me	direct bond	4-MeO-phenyl	oil
69b	SMe	direct bond		153-4
70b	SMe	direct bond		198-200
71b	SMe	direct bond	4-(4-Cl-benzyloxy)phenyl	oil
72b	SMe	direct bond		154-6
73b	SMe	direct bond	4-(2-CN-phenoxy)phenyl	154-8

Cmd	R^2	K	L	m.p. /°C
74b	S(O)Me	direct bond	4-(4-Cl-benzyloxy)phenyl	129-44
75b	S(O)Me	direct bond		157-60
76b	S(O)Me	direct bond	4-(2-CN-phenoxy)phenyl	168-80
77b	SMe	-C(=O)NH-	3,3-diphenylpropyl	132-4

The following compounds of formula Ix, i.e. compounds of general formula I where R^1 is Me, R^2 is OMe and –K-L is positioned at the 3 position of benzene ring M (see Table C), were also prepared by methods analogous to those of the previous Examples.

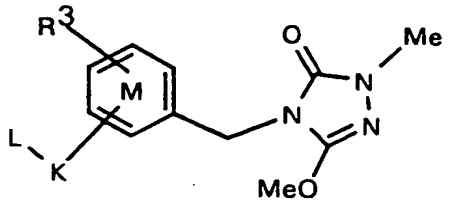


Ix

Table C

Cmp	R^7	R^{7a}	K	L	m.p./°C
2c	Me	H	-C≡C-	trimethylsilyl	oil
3c	Me	Me	-C≡C-	trimethylsilyl	oil
4c	$-CO_2H$	H	-C≡C-	trimethylsilyl	oil
5c	CN	CN	-C≡C-	trimethylsilyl	oil
6c	Me	H	direct bond	4-biphenylyl	132-4

The following compounds of formula Iw, i.e. compounds of general formula I where R^1 is Me, R^3 is Cl, n is 1 and R^7 and R^{7a} are hydrogen (see Table D), were also prepared by methods analogous to those of the previous Examples.



Iw

Table D

Cmp	R^2	R^3	Pos^n of R^3	K	L	Pos^n of K-L	m.p. /°C
1d	OMe	Me	2	-O-	phenyl	4	oil
2d	OMe	Cl	5	$-CH_2O-N=C(Me)-$	3-CF_3-phenyl	2	102-4
3d	OMe	Cl	4	$-CH_2O-N=C(Me)-$	3-CF_3-phenyl	2	114-6
4d	OMe	Cl	5	$-CH_2O-$	2-tolyl	2	85-8
5d	OMe	Cl	4	$-CH_2O-$	2-tolyl	2	85-8
6d	SMe	Cl	5	$-CH=N-O-CH_2-$	4-phenyl	2	127-9
7d	SMe	Cl	5	$-CH=N-O-CH_2-$	3-CF_3-phenyl	2	99-101
8d	OMe	Cl	5	$-CH=N-O-CH_2-$	3-CF_3-phenyl	2	122-5
9d	SMe	Cl	5	direct bond	oxazol-5-yl	2	145-7
10d	OMe	Cl	5	$-CH=N-O-CH_2-$	4-Cl-phenyl	2	130-2
11d	OMe	Cl	5	direct bond	oxazol-5-yl	2	137-9
12d	SMe	Cl	5	-CH=N-O-CH(Me)-	phenyl	2	78-80
13d	OMe	Cl	5	-CH=N-O-CH(Me)-	phenyl	2	oil
14d	SMe	F	4	direct bond	4-Ph-thiazol-2-yl	2	168-9
15d	SMe	F	4	direct bond	4-(4-Cl-phenyl)thiazol-2-yl	2	184-6

Cmp	R^2	R^3	Pos^n of R^3	K	L	Pos^n of K-L	m.p. /°C
16d	OMe	F	4	direct bond	4-Ph-thiazol-2-yl	2	169-71
17d	SMe	F	4	direct bond	4-Me-thiazol-2-yl	2	111-3
18d	S(O)Me	F	4	direct bond	4-(4-Cl-phenyl)thiazol-2-yl	2	200-4

Test Examples

Compounds are assessed for activity against one or more of the following:

Pyricularia oryzae: rice blast

Phytophthora infestans: late tomato blight

Plasmopara viticola: vine downy mildew

Erysiphe graminis f. sp. tritici: wheat powdery mildew

Leptosphaeria nodorum: glume blotch

Aqueous solutions or dispersions of the compounds at the desired concentration, including a wetting agent, were applied by spray or by drenching the stem base of the test plants, as appropriate. Plants or plant parts were then inoculated with appropriate test pathogens and kept under controlled environment conditions suitable for maintaining plant growth and development of the disease. In the case of volatile compounds the plants are covered to hinder loss of the compound. After an appropriate time, the degree of infection of the affected part of the plant was visually estimated. Compounds were assessed on a score of 1 to 3 where 1 is little or no control, 2 is moderate control and 3 is good to total control. At a concentration of 500 ppm (w/v) or less, the following compounds scored 2 or more against the fungi specified.

Pyricularia oryza

31a, 36a, 8b, 20b, 23b, 24b, 25b and 27b;

Phytophthora infestans

8b, 9b and 20b;

Plasmopara viticola;

1a, 2a, 3a, 4a, 16a, 22a, 23a, 24a, 25a, 26a, 30a, 33a, 45a, 48a, 8b, 9b and 15b;

Erysiphe graminis f sp. tritici;

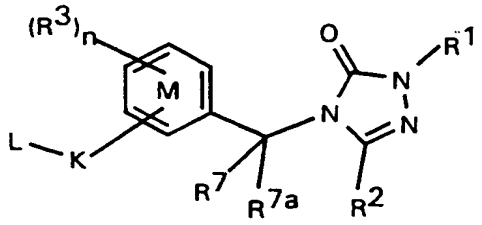
1a, 2a, 3a, 18a, 38a, 39a, 41a, 6b, 24b, 25b and 28b;

Leptosphaeria nodorum.

Compounds 1a, 2a, 3a, 21a, 22a, 28a, 31a, 40a, 47a, 6b, 8b, 17b, 19b, 20b, 22b, 24b, 25b and 27b.

CLAIMS

1 A compound of general formula I



(I)

wherein;

R^1 is optionally substituted alkyl;

R^2 is optionally substituted alkyl, halogen, $-OR^4$, $-SR^4$, $-S(O)R^4$, $-S(O)_2R^4$ or $-NR^5R^6$;

n is 0 to 4;

each R^3, which may be the same or different from each other, is optionally substituted alkyl or halogen;

R^7 and R^{7a}, which may be the same or different are, optionally substituted alkyl, acyl, halogen or cyano;

K is $-O-$, $-S(O)_p-$, $-C(=O)-$, $-NR^8-$, $-CHR^9-A^1(C=A^2)-A^3-$, $-CHR^9-O-N=C(R^{10})-A^4-$, $-C(=O)NR^8-$, $-O-CH_2CH_2O-N=C(R^{10})-$, $-CHR^9O-C(R^{10})=N-$, $-CHR^9S-C(R^{10})=N-$, $-C(R^{10})=N-N(R^8)-$, $-CH=N-N=C(R^{10})-$, $-CHR^9N(R^8)-N=C(R^{10})-$, $-CHR^9N[C(=O)R^{11}]-N=C(R^{10})-$, $-OC(=S)NR^8C(=O)-$, $-CHR^9-C(=A^2)-A^3-$, $-CHR^9CHR^{12}-C(=A^2)-A^3-$, $-CR^{10}=CR^{13}-C(=A^2)-A^3-$, $-C\equiv C-C(=A^2)-A^3-$, $-N=CR^{10}-C(=A^2)-A^3-$, $-CH(OR^{11})-$, $-CHR^9-$, $-CHR^9CHR^{12}-$, $-CR^{10}=CR^{13}-$, $-C\equiv C-$, $-CHR^9O-$, $-OCHR^9-$, $-CHR^9S(O)_p-$, $-S(O)_pCHR^9-$, $-(R^{10})C=N-OCH(R^9)-$, $-C(R^{10})=N-O-$, $-O-N=C(R^{10})-$, $-CHR^9SC(R^{10})=N-NR^8-$, $-CHR^9SC(R^{10})=N-N=CR^{13}-$, $-CHR^9OC(R^{10})=N-N=CR^{13}-$ or a direct bond; where the moiety depicted on the right side of the linkage is attached to L; and

L is optionally substituted alkyl; optionally substituted alkenyl; optionally substituted alkynyl; optionally substituted heterocyclyl; optionally substituted carbocyclyl, or $Si(R^{15})_3$; or one R^3, K and L, together with the phenyl ring M, form an optionally substituted fused ring, which may contain heteroatoms;

where R^4 is hydrogen or optionally substituted alkyl;

R^5 and R^6, which may be the same or different, are hydrogen or optionally substituted alkyl, or R^5 and R^6 taken together with the nitrogen to which they are attached may form a heterocyclyl group, preferably a 5 to 7-membered heterocyclyl group, which may be substituted and may contain other hetero atoms;

p is 0 to 2;

A^1 is -O-, -S-, $-NR^8-$ or $-O-N(R^8)-$;

A^2 is O, S or NR^8;

A^3 is -O-, -S-, $-NR^8-$ or a direct bond;

A^4 is $-NR^8-$, $-OCH_2-$, -N=N-, -(C=O)-, $-CH_2O-$, $-CH_2S-$ or a direct bond;

R^8 is hydrogen, optionally substituted alkyl, optionally substituted carbocyclyl or optionally substituted heterocyclyl;

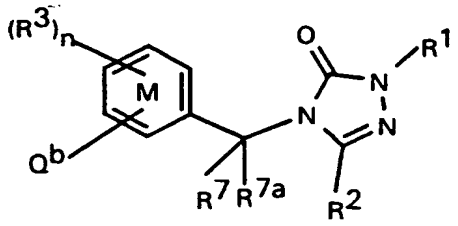
R^9 and R^{12}, which may be the same or different, are hydrogen, optionally substituted alkyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, $-NR^5R^6$, cyano, halogen or nitro;

R^{10} and R^{13}, which may be same or different, are hydrogen, optionally substituted alkyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted alkenyl, optionally substituted alkynyl, acyl, $-OR^4$, $-S(O)_pR^4$, $-NR^5R^6$, nitro, halogen or cyano;

R^{11} is hydrogen, optionally substituted alkyl or optionally substituted carbocyclyl; and

R^{15} is alkyl.

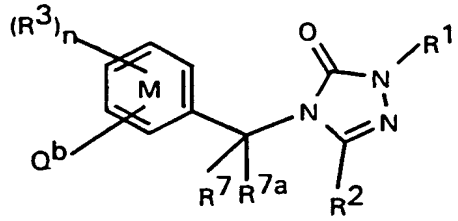
2 A compound of formula II



(II)

wherein Q^b is a leaving group and R^1, R^2, R^3, R^7 and R^{7a} are as defined in claim 1.

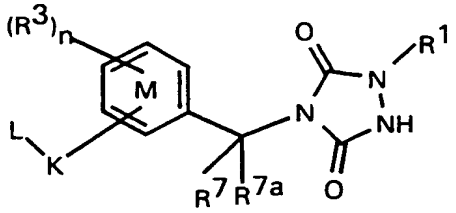
3 A compound of formula II



(II)

wherein Q^b is a halogen and R^1, R^2, R^3, R^7 and R^{7a} are as defined in claim 1.

4 A compounds of formula III



(III)

wherein R^1, R^3, R^7, R^{7a}, L and K are as defined in claim 1.

5 A pesticidal composition comprising compounds as claimed in claim 1 in admixture with an agriculturally acceptable diluent or carrier.

INTERNATIONAL SEARCH REPORT

International Application No
[redacted]GB 98/02238

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C07D249/12 C07D249/14 C07D409/10 C07D417/12 C07D401/12
C07D403/12 C07D405/10 C07D417/10 C07D413/10 C07D471/04
C07F7/10 A01N43/653 A01N55/10

According to International Patent Classification(IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C07D C07F A01N

Documentation searched other than minimumdocumentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 91 12001 A (MERCK & CO., INC.) 22 August 1991 see the whole document, particularly pages 53-61	1-5
X	EP 0 475 898 A (CIBA-GEIGY AG) 18 March 1992 see the whole document	1-5
X	EP 0 412 594 A (MERCK & CO. INC.) 13 February 1991 see the whole document	1-5
X	WO 92 20662 A (MERCK & CO., INC.) 26 November 1992 see the whole document	1-5

-/--

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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"L" document which may throw doubts on priority claim(s) or which is cited to establish the publicationdate of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of theinternational search	Date of mailing of the international search report
23 October 1998	30/10/1998

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Allard, M

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Interi[redacted] Application No
PCT/[redacted]98/02238

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
X	WO 91 18888 A (G.D. SEARLE & CO.) 12 December 1991 see the whole document	1-5
A	WO 96 36616 A (E.I. DU PONT DE NEMOURS AND COMPANY) 21 November 1996 see the whole document	1-5
A	WO 96 26191 A (E.I. DU PONT DE NEMOURS AND COMPANY) 29 August 1996 see the whole document	1-5
A	WO 96 36615 A (E.I. DU PONT DE NEMOURS AND COMPANY) 21 November 1996 see the whole document	1-5

1

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB 98/ 02238

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claims Nos.: not applicable
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

B x II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No. PCT/ GB 98/02238

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Claims Nos.: not applicable

In view of the statement at page 9, line 11, of the description and of the majority of the examples, the search was extended to compounds as defined in the claims, wherein R7 and/or R7a are hydrogen.

This extended search revealed however such a large number of documents affecting the novelty of the claims insofar compounds wherein R2 is an "optionally substituted alkyl" and L-K is an "optionally substituted carbocyclyl" are concerned, that for this aspect of the claims a comprehensive International Search Report is not feasible.

INTERNATIONAL SEARCH REPORT

Inf n on patent family members

Int[illegible]ial Application No
P[illegible]GB 98/02238

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INTERNATIONAL SEARCH REPORT

Information on patent family members

Inter. [redacted] Application No
PCT/[redacted]98/02238

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